made, is enclosed hereto in accordance with 37 C.F.R. § 1.121.

The specification has been amended to reflect an updated status paragraph. A marked-up version of that portion of the specification that has been amended is enclosed hereto, showing the changes made.

Each of the Examiner's rejections is discussed below in the order it was set forth in Paper No. 6.

Rejection Under 35 U.S.C. § 101.

At page 2 of Paper No. 6, the Examiner has rejected claims 12-14 under 35 U.S.C. § 101 asserting that such claims are directed to "non-statutory subject matter." These claims have been cancelled. Accordingly, the applicants submit that the Examiner's rejection is no longer applicable, and its reconsideration and withdrawal are respectfully requested.

Rejections Under 35 U.S.C. § 112.

The Examiner has rejected claims 1, 2, 5-7, 10, and 11 under 35 U.S.C. § 112, second paragraph, asserting such claims are indefinite for use of the phrase "other than." While not necessarily agreeing with the Examiner, claims 1, 2, and 10 have been amended to clarify that the drug included in the oil-in–water emulsion of the claimed composition is not a cannabinoid.

Additionally, claims 5-7 and 11 have been amended so that the acronym "NSAID" is replaced by the full terminology "non-steroidal anti-inflammatory drug."

In view of these amendments, it is respectfully requested that the Examiner reconsider and withdraw his rejection under 35 U.S.C. § 112.

Rejection Under 35 U.S.C. § 103 Based Upon U.S. Patent No. 6,096,728 Taken in View of U.S. Patent No. 5,811,425.

At page 3 of Paper No. 6, the Examiner has rejected claims 1-14 under 35 U.S.C. § 103(a) as being unpatentable (obvious) over U.S. Patent No. 6,096,728 of Collins *et al.* ("Collins"), in view of U.S. Patent No. 5,811,425 of Woods *et al.* ("Woods"). As basis for this rejection, the Examiner applies Collins as follows:

> Collins discloses a composition and method for treating pain and Parkinson's disease, other inflammatory diseases, flurbiprofen and ibuprofen, non-steroidal anti-inflammatory diseases. Collins

steroidal anti-inflammatory drug [(NSAID)] [other than a cannabinoid] but wherein the drug is not a cannabinoid, for use in medicine.

5. (Amended) A composition according to Claim 1, wherein the [NSAID] non-steroidal anti-inflammatory drug is flurbiprofen.

6. (Amended) A composition according to Claim 1, wherein the [NSAID] non-steroidal anti-inflammatory drug is ibuprofen.

7. (Amended) A composition according to Claim 1, wherein the [NSAID] non-steroidal anti-inflammatory drug is a COX-1 or COX-2 inhibitor.

10. (Amended) A method for the treatment of pain which comprises delivering an oil-in-water emulsion containing a systemically active drug [other than a cannabinoid] by the nasal route, wherein the drug is not a cannabinoid.

11. (Amended) A method according to Claim 10, wherein the drug is a [NSAID] non-steroidal anti-inflammatory drug.

Marked-Up Version of Specification and Claims

U.S. Patent No. 09/841,228

In the Specification:

Shown below are the changes to replacement paragraph **[0001]** of the specification marked up to show the changes made. Please note that deletions are indicated by brackets and insertions are indicated by underlining.

[0001] This application is a continuation of International Application No. PCT/GB99/03489, filed October 21, 1999, and published in the English language on May 4, 2000, under International Publication No. WO 00/24373, the disclosure of which is incorporated herein by reference.

In the Claims:

Shown below are the amended claims 1, 2, 5-7, 10 and 11, marked up to show the changes made. Please note that deletions are indicated by brackets and insertions are indicated by underlining.

1. (Amended) A pharmaceutical composition adapted for nasal administration comprising (i) an oil-in-water emulsion and (ii) a drug dissolved in the emulsion, wherein the oil phase comprises a hydroxylated oil and wherein the drug is for systemic delivery and is [also] selected from the group consisting of an analgesic agent, a drug for the treatment of Parkinson's disease, a drug for the treatment of impotence, [or] and a non-steroidal anti-inflammatory drug [(NSAID)], [other than a cannabinoid] but wherein the drug is not a cannabinoid.

2. (Amended) A composition adapted for nasal administration comprising (i) a oil-in-water emulsion and (ii) a drug dissolved in the emulsion, wherein the oil phase comprises a hydroxylated oil and wherein the drug is for systemic delivery and is [also] selected from the group consisting of an analgesic agent, a drug for the treatment of Parkinson's disease, a drug for the treatment of impotence [or] and a non-

> teaches pharmaceutical compositions which are known to be in the form of an emulsion and COX-2 inhibitors. Collins teaches salicylic acid derivatives, propionic acid derivatives, acetic acid derivatives, fenamic acid derivatives, carboxylic acid derivatives, butyric acid derivatives, oxicams, pyrazoles and pyrazalones having similar analgesic and anti-inflammatory properties.

(Paper No. 6 at page 3 (citations omitted)). The Examiner concedes that Collins does not teach a hydroxylated oil. However, the Examiner contends that Woods teaches a hydroxylated oil (castor oil) which, according to the Examiner, "is known in pharmaceutically acceptable emulsions and it is known in the art that the oil provides solubilization of the drug." The Examiner also asserts that Woods teaches pharmaceutical compositions comprising emulsions, vegetable oils, and COX-1 and COX-2. The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the hydroxylated oil of Woods in the composition of Collins, with the expectation of providing a pharmaceutical composition comprising castor oil and a drug dispersed in an emulsion. The applicants traverse this rejection and the arguments provided in support thereof, for the reasons set forth below.

Collins teaches a pharmaceutical composition for treatment of interleukin-1 (IL-1) mediated inflammatory diseases, particularly diseases of the joint. The composition disclosed in Collins contains a controlled release polymer and a proteinaceous IL-1 inhibitor. The controlled release polymer taught for use in Collins may be a bulk erosion polymer, a surface erosion polymer, cellulose, hyaluronan, alginate, collagen, gelatin, albumin, and starches and dextrans. Additionally, the Collins composition may include non-steroidal anti-inflammatory drugs (NSAIDS) and analgesics. The Collins composition does not contain a drug for use in the treatment of impotence.

At Col. 26, lines 33-36, Collins teaches that, once the Collins composition has been formulated, it "may be stored in a sterile vial as a solution, suspension, gel, emulsion, solid, or a dehydrated or lyophilized powder." No specific type of emulsion is described or disclosed. Specifically, Collins does not teach an oil-in-water emulsion in which the IL-1 inhibitor or any of the other additional drugs disclosed in Collins is suspended. Additionally, as the Examiner concedes, Collins does not teach use of a hydroxylated oil, and further does not teach use of an oil-in-water emulsion containing a hydroxylated oil.

Woods teaches a COX-2 inhibitor of a specific structure. Woods teaches that this COX-2 inhibitor can be incorporated into a pharmaceutical composition for a parenteral

injection, including pharmaceutically acceptable sterile aqueous or non-aqueous solutions, dispersions, suspensions, or emulsions, as well as sterile powders. Examples of suitable aqueous and non-aqueous carriers, dilutants, solvents, or vehicles, disclosed in Woods include water, ethanol, polyols, vegetable oils (such as olive oil), and injectable organic esters. Liquid dosage forms for oral administration are also disclosed and include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs. Woods teaches that, in addition to the active compounds, the liquid dosage forms may contain inert dilutants. A long list of such dilutants is provided, and includes water, ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethyl formamide, and oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame). Woods does not make a specific disclosure of any particular type of emulsion, and certainly does not specify that the COX-2 inhibitor of Woods can be suspended in an oil-in-water emulsion. Additionally, there is no disclosure in Woods of an oil-in-water emulsion that uses a hydroxylated oil.

In order to establish a case of *prima facie* obviousness, the Examiner must demonstrate (i) that the suggested combination teaches or suggests each element of the claimed invention; (ii) that there is some motivation in the art for a person of ordinary skill to make the combination as proposed by the Examiner; and (iii) that a person of ordinary skill would have had a reasonable expectation that such modification would be successful.

The Examiner has failed to establish a *prima facie* case of obviousness based upon her Collins-Wood combination. First, the Collins-Wood combination does not teach or suggest each element of the claimed invention. Collins does not teach an oil-in-water emulsion in which the disclosed optional NSAIDS or analgesics are suspended. The disclosure of Woods does not remedy this deficiency, as Woods does not teach any specific type of emulsion, let alone an oil-in-water emulsion in which the disclosed COX-2 inhibitor is suspended, and in which castor oil is used. In contrast, the present invention is a pharmaceutical composition adapted for nasal administration containing an oil-in-water emulsion and a drug dissolved in the emulsion. The oil phase of the oil-in-water emulsion is a hydroxylated oil. Accordingly, as the Collins-Woods combination does not teach or suggest each element of the claimed invention, it cannot be the basis of a finding of *prima facie* obviousness.

Additionally, a person of ordinary skill would have had no motivation to make the Collins-Wood combination as suggested by the Examiner, nor is there any suggestion that such combination would give rise to successful results. Neither Collins nor Woods discloses use of

oil-in-water emulsions suitable for compositions for nasal administration. Collins discloses preparations that may contain anti-inflammatory compounds for oral or injectable administration. *See,* Col. 34, line 30 to Col. 35, line 30. Similarly, Woods describes oral formulations. Accordingly, a person seeking to make an oil-in-water emulsion pharmaceutical composition suitable for nasal administration would not seek out the teachings of either Collins or Woods and combine them to arrive at the present invention, nor would he reasonably expect such combination to give rise to a successful oil-in-water emulsion, as it is well known in the art that suitable vehicles for oral administration are not necessarily effective if applied to compositions for nasal administration.

Accordingly, for the reasons set forth above, it is respectfully requested that the Examiner reconsider and withdraw her 35 U.S.C. § 103(a) rejection.

CONCLUSION

In light of the foregoing amendments, it is respectfully submitted that claims 1-11 are fully compliant with 35 U.S.C. § 112. Moreover, in view of the above remarks, it is submitted that all of the pending claims patentably distinguish over the prior art cited by the Examiner. Consequently, it is respectfully requested that the Examiner reconsider and withdraw her rejections with respect to these claims, and allow the claims at the earliest possible opportunity.

Respectfully submitted,

STANLEY STEWART DAVIS *et al.*

11 december 2002 By: Kristyne a. Bullock
(Date)

KRISTYNE A. BULLOCK
Registration No. 42,371
AKIN, GUMP, STRAUSS, HAUER & FELD, L.L.P.
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7086
Telephone: (215) 965-1200
Direct Dial: (215) 965-1348
Facsimile: (215) 965-1210
E-Mail: kbullock@akingump.com

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Enclosure